Early Diagnosis of Chronic Kidney Lesions.

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EARLY DIAGNOSIS OF CHRONIC KIDNEY LESIONS.[1]

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What means have we at present to determine that a patient has some chronic disease of the kidneys?

What is the relative value of these agents, and how far can they be depended upon in the diagnosis of individual cases?

These are questions that are certainly very important to every one who, in any way, bears relation to these diseased conditions, and should be answered as far as it may be possible for us to answer them.

Let us first look at the relative value of albumin in the urine as a diagnostic sign of disease. At one time the discovery of albumin in this excretion was considered an almost fatal omen, but now the area of its deadly significance has been so circumscribed in many particulars, that it no longer is pathognomonic of even a serious lesion of the kidneys. Indeed, we are now looking upon this excrementitious product in two widely different ways, as physiological and pathological. So far as we now know, a certain small quantity of albumin in the urine is not incompatible with health, even though it occurs at frequent intervals for a long period of time. Generally, it is true that this so-called physiological product is the result of abnormal physical conditions; as, for example, the consequence of severe bodily exercise or undue mental strain. Persons passing such small quantities of albumin for months, or even years, have had a sudden cessation of this excretion and have never more been so disturbed, and, consequently, it could not have been the result of serious kidney lesions. The fact, however, that these small quantities of albumin occur often in other well-recognized pathological conditions in parts remote from the kidneys, is very significant, and points, if in any direction, toward a common pathological condition involving large areas of the body. When the facts are all in, we need not be surprised if this so-called physiological albumin is a factor in the early diagnosis of widely diffused pathological changes, which occur in common with kidney lesions in the initial stage. Our knowledge, as yet, is too meagre

[1] Read before the Mississippi Valley Medical Society, September 12, 1889.

however, to affirm this conjecture, and we must at present regard this excretion in the light of suspicion without attaching much importance to its diagnostic value.

Pathological albumin, on the other hand, has received too much credit as a guide to structural renal diseases, and within the last few years has lost its former dread and cannot longer be considered as pathognomonic of kidney lesions. That it occurs often in these diseases cannot but be affirmed by all careful observers; still the cases are quite numerous that either do not present this diagnostic sign at all during the course of the disease, or fail to do so at longer or shorter intervals during the progress of very destructive changes in these organs. Post-mortems have developed the fact that many persons have died from evident kidney diseases without the fact becoming apparent by careful examinations of the urine for albumin at frequent intervals. Again, albumin is found in the urine in large amounts without necessarily emanating from diseased kidneys, such as is caused by the hydrostatic variation in these organs incident to cardiac or lung lesions, pressure of tumors, or from irritation in the central nervous system. Albumin may also occur as the result of systemic disturbances, such as the infectious fevers, and may pass away with the general convalescence, or may remain as an evidence of a permanent lesion. Some local disorders involving the urethra, bladder, or ureters, furnish often abundant evidence, if not recognized, of serious destruction of the kidneys,—as gonorrhœa, cystitis, and other inflammatory diseases.

In well-marked Bright's disease, albumin generally is found some time during its course, yet the variation of this product makes diagnosis often uncertain, if this were the only means at our command. This albumin varies from day to day, being great at times and almost absent at others; occurring in the morning urine and not in the evening, or the reverse may be true. It may be found in some varieties of Bright's disease, and scarcely if ever in other forms of this malady. The albumin most sought in these tests is common to all the cases included under chronic Bright's disease, and is also common to the acute forms of the same, and cannot therefore be held as a definite diagnostic sign of any of these diseases, or as an unvarying factor in differentiation.

As Bright's disease is, according to my belief, the result of constitutional disturbances which involve at first nutrition and thereby the general integrity of the tissues and consequently of the kidneys, it is evident that by the time albumin makes its appearance in the urine the disease has, in all chronic forms, gone on for some time, and while we must acknowledge the importance of albumin in the urine at this time as quite conclusive, with the exceptions noted, still at this stage many of such patients die after a series of explosions, which intervene at longer or shorter intervals, and consequently the knowledge so gained is of very

little value to the patient, however interesting it may be to the scientific physician.

If we look for casts, in our effort to evade a fatal malady, we find that we are in equally as great a dilemma, since casts are the consequence of the uncertain conditions already referred to, with additional uncertainties. Casts may be found very abundant in the beginning of serious lesions of the kidneys, or very few in number. They may be absent altogether. If casts are found, albumin has already appeared in the urine and given its warning, and consequently casts must rank second as evidence in the early diagnosis of chronic kidney lesions. The character of the cast often, no doubt, enables us to differentiate between the varieties of chronic Bright's disease, and may give knowledge also of the length of time the inflammatory conditions have existed, all of which again profits the patient but very little. We have in all cases to deal with a chronic inflammation which is diffuse, and while it involves different tissues in the beginning, and has often a different history, still very soon enough of the kidney structure is involved or encroached upon to produce in all cases the same clinical results, and so far as the early differentiation of these varieties is concerned, it is of scientific value rather than an aid in our present need.

Several papers have been written during the past two years in support of the specific gravity of the urine as a diagnostic sign of chronic kidney lesions, and some notion akin to this has crept into books bearing the names of prominent authors. The specific gravity of the urine could mean nothing more than the relative measure of all the elements held in solution. Therefore, if a urine was of relatively low specific gravity, it might mean that the quantity of water passed was very great, or that the products held in solution were few. These products might bear almost any relation to each other; that is, the urine might be loaded with phosphates and be relatively quite heavy, while the quantity of urea, carbonate of ammonium, uric acid, and other suspended salts might be very small in amount. If it be true that the specific gravity bears any relation to diseased kidneys, it must be the mean specific gravity of many often-repeated examinations of known quantities of urine for given times, as it would then indicate something of a measure of the total toxicity of the salts held in the blood, or the permeability of the kidneys. My experience has been that urine passed by patients with evident kidney lesions is frequently of relatively high specific gravity, due generally to large quantities of the phosphates, or carbonates, or both. If often-repeated examinations of urine from the same patient should show, however, a constantly low specific gravity for normal quantities of urine, it would then point to some disturbance in the excretory organs, or that some one or more of the salts were not produced in normal quantities in the blood. Since, however, urea—if not the only product excreted

having toxic influence—is diminished in cases of serious lesions of these organs, and generally is the dominant salt, it would be fair to state, that all other products being excreted in their normal quantities, the urine would have a more or less relatively low specific gravity when compared with the known daily quantity of urine excreted. The specific gravity without this knowledge would be of little, if any, value in the diagnosis of such lesions. And none of the writers, so far as I am aware, have taken these conditions into consideration.

No diagnosis of these lesions can be complete without a perfect knowledge of the outward symptoms of the patient, and the value of any other knowledge must depend upon a constant relation which is found to exist between these physical conditions of ill health and the defect in excretion. If it were possible, in other words, for a patient to pass albumin and casts for years and no signs of ill health intervene, it would go far to disprove the value of these as a diagnostic sign of pathological conditions in that individual, and if this were the rule no importance could be attached to their excretion in the urine. It is fortunate, therefore, that during the time, at least, that these products are being thrown out, the patient has well-marked symptoms of ill health. It is still more fortunate that these outward manifestations of disease are the first presented, and are more or less constant, not only in the individual, but for the whole group so passing albumin and casts. While there are occasional exceptions to this rule that make differential diagnosis difficult in the beginning, still there is such a constant association as to be in great part relied upon at this stage of the disease. These symptoms are dyspnœa, vertigo, blindness, nausea, vomiting, swelling of extremities or face, twitching of any or all muscles, a feeling of being constantly tired without exertion, pain in intercostal region or extremities, headache, smarting pain on passing water, with frequent desire to urinate, a constant tendency to inflammations of serous membranes, with frequent evidence of some form of these inflammatory results upon careful physical examination. All of these symptoms go to make a picture of typical cases of persons suffering from these lesions, yet the presence of two or more constant symptoms, if accompanied with albumin and casts, will complete with accuracy the diagnosis of the case. The association, therefore, of these external evidences constantly with the excreted evidence, leads us to know to a reasonable certainty that one group being found in such well-marked cases, the other is sure also to be present. In milder cases, however, the excretory evidence is not always found, still these patients are suffering with evident diagnostic signs of diseased kidneys, and faithful examinations for a long time will generally be rewarded by this additional confirmatory evidence. At this stage, however, many of our patients die, and it seems sad indeed that so much effort has been expended without a greater benefit accruing to the sufferer.

It was at this point that more than five years ago I began to inquire why it was that patients answering in many respects those with marked kidney lesions, did not confirm this diagnosis by also passing albumin and casts, and what was the diagnostic sign that should bind these two groups of patients in one common class.

Authorities at this time stated that excess of urea was found in the blood of patients dying from these lesions, and that a lessened quantity was daily excreted in cases having the additional evidence of albumin and casts, and yet no careful records, so far as I know, had been made of the pathological variations of urea for definite quantities of urine for twenty-four hours, and extended at frequent intervals for months and years, for this class of patients. Authorities even now put no especial stress on the amount of urea as a diagnostic sign of chronic kidney lesions. In reviewing my records of cases for these years, I find that not a case appears in which other evidence, as albumin and casts, was present, that has not shown a constantly diminished average quantity of urea excreted in twenty-four hours, and I now regard this evidence as constant, whereas the others are variable.

Diminished quantities of urea excreted for twenty-four hours and continued for some months, in persons otherwise healthy and living on a mixed diet, can be taken as pathognomonic of kidney lesions, and this condition may exist in individuals giving no other evidence in the urine of such disease. After months of careful and painstaking efforts we may have our curiosity gratified by finding that the patient passes albumin or casts for the first time. If several such patients have followed the same doleful road and we have found albumin at frequent intervals in pathological quantities, and after their deaths have made post-mortems that demonstrated chronic nephritis, we can then say, we think with great force, that this pathognomonic evidence that exists together with albumin is also the evidence of serious conditions that precede these fatal cases. If, now, these patients who do not pass albumin or casts have other pronounced symptoms, such as vertigo, nausea, general weakness, œdema, as in well-marked cases, with absence of all other signs of disease, after careful examination, we would have the right to affirm that there was a very intimate relation between these two classes of patients, if they are not indeed, in other respects identical. I am as certain as I can be of anything, after careful study and something over a thousand examinations, that this relation does exist, as I have verified it many times among these patients; having had patients after two or three years, with all outward evidences of these lesions, suddenly begin passing albumin and casts and finally die of what a post-mortem showed to be chronic nephritis.

I do not know whether urea is the only irritating agent in these cases, and that creatin or creatinine be the form in which it finally produces

its injurious results, or whether it is simply the expression of a constitutional disease which is in common with the kidney lesions. What I do know is, that there is always a relation existing, as shown by clinical observation and careful tests, between small eliminated quantities of urea and the general ill feeling of the patient, and that this same relation holds equally good whether patients are now passing albumin and casts or whether they are free from this symptom, and that the only thing needful in urinary tests is a record of these diminished quantities of urea for twenty-four hours, for long periods of time, together with the symptoms. It is very remarkable that these two factors, *i. e.*, the symptoms and the knowledge of urea, should be interchangeable, *i. e.*, if a patient passes constantly small quantities of urea, living on a mixed diet and otherwise healthy, we can predict with certainty that such patient will complain of some of the prominent symptoms before referred to in this paper, as belonging to chronic lesions of the kidneys, even months and years, it may be, before other urinary diagnostic signs make their appearance. So well established do I consider these deductions, that I deem it no longer necessary when such a patient presents himself, to wait until albumin and casts are passed, to begin a vigorous line of treatment, to try, if possible, to avert the result that often obtains otherwise after a longer or shorter time.

This brings me to another and very valuable means at our command so thoroughly to circumscribe this disease that we know it can be no other; and I now refer to treatment. If there be a doubt left concerning the diagnosis of a case passing constantly ten or twelve grammes of urea in twenty-four hours, and otherwise healthy, with the accompanying signs of vertigo, nausea, general weakness, pallor, and dyspnœa, a few doses of a saline cathartic will effectually dispel it, as the remedy has never played any important curative place in anæmia and general weakness from other causes. Such a patient after free evacuation of the bowels will become steady, have a better appetite, lose the dyspnœa, and become stronger. If now a diuretic be given, and the renal structure is not too much involved, the patient will pass after a few days an increased quantity of urea, and just in proportion as the urea increases will the bad symptoms be ameliorated. Would we treat patients with these symptoms from other causes in that way? What makes the proof doubly strong is the fact that many of these patients have gone the rounds for years among doctors who have tried to redden their lips with iron and other tonics, but still the same pallor existed, and because no casts or albumin could be found in the urine at one or two examinations they put a pessary into the vagina, or discovered a deep rectal ulcer. A climacteric must be passed, or puberty was involved. The patient had dyspepsia or pernicious anæmia, that with the burden of drugs grew no better. What is most gratifying, is, that after proper treatment many

of these patients, who answer in all other respects to well-defined Bright's disease, grow better and, according to all tests, are apparently well. A few remain about as when first found, and a still smaller class pass albumin and casts and die according to the rule with such cases.

In papers read before the Indiana Medical Society, in 1886 and 1887, and again before the Mississippi Valley Medical Society in 1888, I stated that I believed, that from all the evidence that I then had, Bright's disease was not simply a lesion in the kidneys, but that more or less extensive areas were involved primarily, and that the kidney lesions were simply a part of this general condition. I am glad to say that there is a growing tendency among the profession to this view, and when all the facts are in concerning these constitutional disturbances, we will know more of other diagnostic signs that precede the more serious illness. If it be true, as I believe and have advocated in these papers, that extensive inflammatory changes take place in serous membranes at or before the time the kidneys are involved, then the evidence in other regions of the body would lead to the conclusion that if the kidneys are not so diseased, such a condition was threatening or probable, or at least possible, and we should then advance one more step in the diagnosis of this deadly disease. It is quite probable that some irritant or irritants first appear in the blood to affect nutrition and thus bring about these extensive changes, but I am unable to affirm this conclusion. What I do know is, that at or preceding the time these changes are taking place in the kidneys, evidence may often be found in other regions of the body of inflammation of serous membranes, and that, associated with these phenomena, urea is eliminated during twenty-four hours in much smaller quantities than in health.

I therefore, in conclusion, present the following synopsis, which, so far as pertains to my efforts in these investigations, I submit for proof or disproof.

Albumin in the urine probably means disease somewhere in the body. In so-called physiological quantities it probably may be referred to disease removed from the kidneys, and is as transient as the cause. In pathological quantities it signifies either inflammation external to the kidneys or a lesion of these organs. Many patients do not pass albumin with evident kidney lesions. Albumin is inconstant and bears no relation to the extent of the lesion, but when present must be respected as a prominent factor in diagnosis. It generally makes its appearance a long time after other well-marked symptoms have existed, and the disease is grave when it exists in pathological quantities and should not therefore be waited for.

Casts bear an intimate relation to albumin, but appear later. They are strong proof of renal inflammation, as they carry, usually, a part of its epithelium. Differential diagnosis of the varieties of kidney lesions

Fifty Cases passing Small Quantities of Urea that have been under Observation from Two to Five Years.

Table I.—*Patients passing large quantities of albumin with casts and excreting constantly small quantities of urea, who finally die.*

No.	Age.	Sex.	Years under observation.	Examination of urine.									Prominent symptoms.	Complications.	Treatment.	Termination.
				Number of examinations.	Aver. ounces in 24 hours.	Albumin.	Casts.	Aver. specific gravity.	Aver. per cent. of urea.	Aver. grams of urea in 24 hrs.	Min. grams of urea in 24 hrs.	Max. grams of urea in 24 hrs.				
1	56	M.	...	10	16	Yes	Yes	1018	2½	12	7	14	General weakness, headache, nausea, vertigo, dyspnœa, swelling of extremities.	During course of disease had pleurisy.	Saline cathartics, diuretics, sudorifics	Post-mortem showed chronic interstitial nephritis.
2	35	F.	...	8	22	Yes	Yes	1012	2	13	10	15	Dyspnœa, pain in intercostal region, insomnia, nausea, swelling of face and extremities, and finally of abdomen.	Hypertrophy of heart.	Saline cathartics, diuretics, tapping abdomen, sudorifics	Post-mortem showed chronic interstitial nephritis.
3	38	F.	...	12	18	Yes	Yes	1015	2	11	7	18	Pain in intercostal region, twitching of muscles, nausea, vertigo, general weakness, swelling of extremities.	None.	Saline cathartics, diuretics, anodynes, sudorifics.	Post mortem showed chronic parenchymatous nephritis.
4	48	M.	...	6	25	Yes	Yes	1018	2	15	11	15	Dyspnœa, general weakness, loss of appetite, pain in intercostal region, vertigo, swelling of lower extremities.	Periodical attacks of asthma.	Saline cathartics, diuretics, sudorifics, stimulants.	No post-mortem allowed.

TABLE II.—*Patients passing neither albumin nor casts, but a constantly diminished average quantity of urea, who finally die.*

No.	Age.	Sex.	Years under observation.	Examination of urine. Number of examinations.	Aver. ounces in 24 hours.	Albumin.	Casts.	Aver. specific gravity.	Aver. per cent. of urea.	Aver. grams of urea in 24 hrs.	Min. grams of urea in 24 hrs.	Max. grams of urea in 24 hrs.	Prominent symptoms.	Complications.	Treatment.	Termination.
5	65	.	...	10	26	No	No	1013	1½	14	4	24	Has intercostal pain, general weakness, vertigo, blindness, nausea, irritable heart, dyspnœa, swelling of extremities.	Endarteritis; finally became insane.	Saline cathartics, pil. nitro-glycerin, sudorifics, hypnotics.	Post-mortem showed endarteritis of large arteries with parenchymatous nephritis.
6	57	M.	...	13	34	No	No	1012	1½	15	12	21	Numbness of lower extremities, vertigo, general weakness, pain in chest, headache, insomnia, twitching of muscles.	No other disease could be detected	Saline cathartics, diuretics, sudorifics, stimulants.	No post-mortem allowed, but died from evident uræmia.
7	70	M.	...	8	30	No	No	1010	2	12	8	20	General weakness, vertigo, nausea, dyspnœa, symptoms have continued for several years.	No other organic lesions discovered.	Digitalis, cathartics, stimulants at times.	No post-mortem; died from apoplexy with evident kidney lesions.

TABLE III.—*Patients passing constantly small average quantities of urea, but for several months unaccompanied by albumin or casts, who then pass albumin and casts, and ultimately die.*

No.	Age.	Sex.	Years under observation.	Examination of urine. Number of examinations.	Aver. ounces in 24 hours.	Albumin.	Casts.	Aver. specific gravity.	Aver. per cent. of urea.	Aver. grams of urea in 24 hrs.	Min. grams of urea in 24 hrs.	Max. grams of urea in 24 hrs.	Prominent symptoms.	Complications.	Treatment.	Termination.
8	46	F.	...	9	32	Yes	Yes	1011	1½	13	5	19	Had headache, vertigo, nausea, general weakness, dyspnœa, pain in intercostal region, slight swelling of limbs.	Insanity: no other organic lesions discoverable.	Digitalis, sudorifics, anodynes, hypnotics.	No post-mortem allowed, but died with evident kidney lesions.
9	60	M.	...	16	40	Yes	Yes	1016	1¼	15	7	30	Dyspnœa, exhaustion, constant pain in right side of face, insomnia, pain on passing urine.	No other organic disease could be found.	Nitro-glycerin, saline cathartics, sudorifics, quinine.	None allowed, but died from evident uræmia.
10	65	M.	...	10	72	Yes	Yes	1014	¾	16	19	14	Intercostal pain, exhaustion, nausea, insomnia, extreme dyspnœa at times; passed small calculi frequently.	No other disease discoverable.	Nitro-glycerin, saline cathartics, sudorifics, hypnotics.	Post-mortem: parenchymatous nephritis, with pelvis of kidney filled with calculi.

TABLE IV.—*Patients who pass a diminished average quantity of urea accompanied occasionally by albumin and casts, who partially or wholly recover.*

No.	Age.	Sex.	Examination of urine. Years under observation.	Number of examinations.	Aver. ounces in 24 hours.	Albumin.	Casts.	Aver. specific gravity.	Aver. per cent. of urea.	Aver. grams of urea in 24 hrs.	Min. grams of urea in 24 hrs.	Max. grams of urea in 24 hrs	Prominent symptoms.	Complications.	Treatment	Termination.
11	29	M.	2	14	24	Yes	Yes	1017	2	14	7	21	Extreme œdema in legs to body, extreme dyspnœa, insomnia, vertigo, had several previous attacks; pulse 120, temp. 100° at first visit.	No other discoverable lesion.	Nitro-glycerin, diuretics, sudorifics, saline cathartics.	Patient recovered in 4 months, but has tendency to relapse on exposure
12	20	F.	4	20	34	Yes	Yes	1012	$1\frac{1}{2}$	14	9	21	Constant headache, nausea, pain in intercostal region, swelling of extremities, vertigo, general weakness.	Chorea in right leg, no other evidence of disease.	Nitro-glycerin, sodii bromidi, diuretics, sudorifics.	At one time was apparently well, but is now worse.
13	30	F.	5	10	38	Yes	Yes	1016	1	11	8	24	Vertigo, nausea, slight swelling of extremities, exhausted, pale, dyspnœa on slight exertion, painful micturition.	No other evidence of disease.	Diuretics, nitro-glycerin, sudorifics, saline cathartics.	Had child 2 years ago without accident, but is now not so well.
14	43	F.	5	12	25	Yes	Yes	1014	$1\frac{3}{4}$	12	7	21	General exhaustion, headache, vertigo, nausea, intercostal pain, smarting pain on passing urine.	Had rectal ulcer, but same symptoms continued after it was healed.	Diuretics, saline cathartics, sudorifics.	Patient greatly improved after several relapses.
15	36	F.	4	10	30	Yes	Yes	1018	$1\frac{1}{2}$	14	7	20	Pain in back, headache, very nervous with irritable heart, losing flesh; symptoms had continued for long time.	Careful examination showed no other disease.	Diuretics, sudorifics, saline cathartics	Patient has had child since, and has wholly recovered.
16	37	F.	5	15	32	Yes	Yes	1020	$1\frac{1}{4}$	12	6	21	Vertigo, insomnia, intercostal neuralgia, nausea; patient was most of time in bed from exhaustion for six months previous.	Could find no other evidence of disease.	Nitro-glycerin, sudorifics, saline cathartics.	Patient now apparently well, and has been so for more than a year.
17	56	M.	4	6	20	Yes	Yes	1018	3	18	14	28	Headache, nausea, general weakness, irregular pulse, insomnia, slight swelling of extremities.	No other organic lesions discoverable.	Saline cathartics, nitro-glycerin, sudorifics, digitalis.	Patient at last report was apparently well.
18	30	F	4	12	28	Yes	Yes	1020	2	17	7	27	Exhaustion, weakness, headache, nausea, swelling of hands, painful micturition, symptoms had continued for two or three years previous.	No complications discoverable.	Saline cathartics, nitro-glycerin, sudorifics.	Patient after several relapses is now apparently well.

19	32	F.	5	10	32	Yes	Yes	1021	2	18	6	33	Pain in intercostal nerves, dyspnœa, vertigo, nausea, weakness, swelling of extremities, numbness of extremities, painful micturition.	Had three attacks of pelvic cellulitis; had periodical asthma may fever.	Nitro-glycerin, saline cathartics, sudorifics, anodynes.	Patient is now apparently well.
20	34	F.	4	14	38	Yes	Yes	1021	$13\frac{1}{4}$	19	10	30	Constant pain in intercostal region, exhaustion on exertion, œdema of the eyelids, headache, nausea, vomiting, swelling of feet.	No other organic disease present.	Nitro-glycerin, saline cathartics, sudorifics.	Patient has been apparently well for a year past.
21	41	M.	4	6	24	Yes	Yes	1019	$13\frac{1}{2}$	11	5	19	General weakness, vertigo, nausea, slight œdema of extremities, intercostal neuralgia; symptoms have continued for a long time.	No complications discoverable.	Saline cathartics, nitro-glycerin.	Patient rapidly recovered, and has been well since.
22	21	F.	3	8	30	Yes	Yes	1020	$13\frac{1}{4}$	12	7	16	Has lost flesh for six months; been treated for other diseases; has nausea, vomiting, vertigo, slight œdema of extremities, insomnia	Has no other discoverable disease	Saline cathartics, nitro-glycerin, sudorifics.	Patient after relapses is now apparently well.
23	54	M.	2	6	28	Yes	Yes	1018	2	17	13	30	Pain in side, dyspnœa on slight exertion, headache; had symptoms for more than a year when first seen.	No other organic lesion discoverable.	Nitro-glycerin, saline cathartics.	Patient recovered rapidly, and is now well.
24	40	F.	2	6	32	Yes	Yes	1015	2	19	14	25	Dyspnœa, intercostal neuralgia, vomiting; hands, face, and extremities œdematous; exhaustion; large quantity of albumin.	Otherwise healthy	Nitro-glycerin, saline cathartics, sudorifics.	Had child 1 year afterward without accident, and is now apparently well.
25	25	F.	2	8	24	Yes	Yes	1017	$21\frac{1}{2}$	18	10	26	Headache, nausea, exhaustion, œdema of extremities, intercostal neuralgia.	Had pelvic cellulitis 2 years ago, had puerperal convulsions last June; mitral murmur.	Nitro-glycerin, sudorifics, anodynes, saline cathartics.	Patient is now apparently well, except valvular lesion.
26	24	M.	2	6	16	Yes	Yes	1020	3	16	14	17	Vertigo, pain in side, nausea; been sick for several months previous; treated for various diseases.	Had no other discoverable lesions	Nitro-glycerin, saline cathartics, sudorifics.	Patient is very much improved, but not well.
27	24	F.	2	8	34	Yes	No	1019	1	10	6	22	Extreme dyspnœa, vertigo, general weakness, extreme œdema of extremities; face also swollen; painful micturition.	Had no other evidence of disease	Nitro-glycerine, sudorifics, saline cathartics, potassii bicarb.	Patient rapidly recovered, and is now well
28	57	M.	2	6	38	Yes	No	1020	$11\frac{1}{2}$	17	14	25	Great dyspnœa, extremities much swollen; had had such explosions for last five years previous to treatment.	Had chronic pleurisy on both sides with effusion.	Nitro-glycerin, sudorifics, saline cathartics, alcoholic stimulants.	Patient still not much improved.

TABLE V.—*Patients who passed small average quantities of urea, having the prominent symptoms in the other cases, who, under same treatment, recovered.*

No.	Age.	Sex.	Years under observation.	Examination of urine. Number of examinations.	Aver. ounces in 24 hours.	Albumin.	Casts.	Aver. specific gravity	Aver. per cent. of urea.	Aver. grains of urea in 24 hrs.	Min. grains of urea in 24 hrs.	Max. grains of urea in 24 hrs.	Prominent symptoms.	Complications.	Treatment.	Termination
29	27	F.	5	20	38	No	No	1016	1½	17	1	31	Headache, nausea, exhaustion, pale, losing flesh, slight œdema of extremities, vertigo, dyspnœa.	No evidence of other organic lesions.	Nitro-glycerin, saline cathartics, sudorifics.	Patient gradually recovered after relapses, and is now well.
30	26	F.	8	16	40	No	No	1015	1½	18	8	33	General weakness, no œdema, dyspnœa on slight exercise, intercostal pain, headache, "nervous;" weight normal.	No organic lesions discovered.	Nitro-glycerin, saline cathartics, anodynes.	Married, and had babe since without accident, and is now well.
31	45	F.	4	21	48	No	No	1020	1	15	14	38	Irritable heart, headache, dyspnœa; symptoms had existed for several years; appetite good.	No other evidence of disease.	Nitro-glycerin, saline cathartics.	Grew gradually better; had child over a year ago without accident.
32	30	M.	4	10	36	No	No	1016	1½	16	12	26	Constant pain in head and limbs for several months; exhaustion, nausea occasionally, painful micturition, urine very acid.	No other disease discoverable.	Diuretics, saline cathartics.	Patient now apparently well.
33	39	M.	4	12	40	No	No	1015	1¼	15	9	28	Painful micturition, exhaustion, pain constantly in left side, general weakness; symptoms had continued for several months.	Impotence for years previous	Nitro-glycerin, saline cathartics.	Impotency no better; all other symptoms relieved.
34	70	M.	4	8	25	No	No	1018	1¼	16	7	27	Was confined to bed from extreme exhaustion when first saw him; dyspnœa, headache, nausea, œdema of extremities.	No other disease discoverable	Diuretics, saline cathartics, sudorifics.	Made rapid recovery, and is now well.
35	41	F.	4	20	26	No	No	1018	1½	12	5	28	Headache, insomnia, exhaustion, nausea at intervals, slight œdema of extremities, painful micturition.	Periodical "sick headaches."	Diuretics, saline cathartics, nitro-glycerin.	Is apparently well.
36	36	M.	4	14	25	No	No	1017	2	15	9	28	For two years had been constantly having pain in stomach and intercostal region; losing flesh, vertigo, exhaustion.	Chronic gastritis; no other disease discoverable.	Nitro-glycerin, saline cathartics, sudorifics	Grew rapidly better, and is now apparently well
37	30	F.	4	16	52	No	No	1015	½	12	7	24	Intercostal pain, headache, exhaustion; other treatment for months has not relieved; vertigo, slight œdema of extremities.	No complications	Diuretics, saline cathartics.	Got much better; got wet, and relapsed; now apparently well.
38	45	F.	4	10	21	No	No	1015	1½	11	5	23	Vertigo, exhaustion, headache, œdema of feet and limbs, "nervous;" symptoms continued for several months previous	No complications discoverable.	Nitro-glycerin, saline cathartics	Tests showed a much larger average quantity of urea, and patient is better.

39	36	F.	4	21	34	No	No	1016	$1\frac{1}{4}$	13	4	25	Palpitation, very "nervous," exhaustion, vertigo; hands tremble on slight exertion; swelling of feet and limbs.	Well nourished, and no complications.	Nitro-glycerin, saline cathartics, sodii bromidi.	Patient improved rapidly, and is now well.
40	15	F.	3	8	50	No	No	1018	$\frac{4}{5}$	12	12	24	Vertigo, nausea, intercostal pain, exhaustion, dyspnœa on slight exertion, headache, pale.	Other functions normal.	Nitro-glycerin, saline cathartics.	Is now apparently well.
41	68	F.	3	12	30	No	No	1017	$1\frac{4}{5}$	16	10	22	Headache, nausea, vomiting, vertigo, exhaustion; compelled to take bed often.	No other lesions.	Nitro-glycerin, anodynes, saline cathartics.	Well for one of her age.
42	40	M.	3	14	24	No	No	1018	$2\frac{2}{5}$	17	17	23	Headache and backache almost constantly; intercostal pain, exhaustion, vertigo, occasional nausea; unable to work much of time.	No other disease discoverable.	Nitro-glycerin, saline cathartics, other remedies had failed.	Improved from first, and is at this date well.
43	38	F.	3	18	2	No	No	1021	2	16	7	22	Nausea, headache, itching, vertigo, intercostal neuralgia almost constantly; had scarlet fever two years previous, and symptoms began then.	None discoverable	Nitro-glycerin, saline cathartics, sudorifics.	Is now apparently well.
44	75	M	3	14	48	No	No	1020	$1\frac{1}{4}$	18	11	23	Limbs swollen to body, extreme dyspnœa, intercostal neuralgia, headache, exhaustion; appetite good; pulse irregular; heart slightly enlarged.	No heart murmur, well nourished; no other evidence of disease.	Nitro-glycerin, saline cathartics, sudorifics, anodynes	Rapidly recovered from bad symptoms, and is now comfortable.
45	25	F.	2	8	100	No	No	1008	$\frac{1}{25}$	10	5	27	Intercostal neuralgia, extreme œdema of legs, pale, menstruation stopped, hands and feet œdematous, vertigo; complained for several months previous.	Unmarried; not pregnant; no murmur; well nourished; no other evidence of disease.	Saline cathartics, sudorifics, nitro glycerin.	Recovered in 5 weeks, has had no relapse, and is now well.
46	61	M.	2	10	41	No	No	1017	$1\frac{1}{25}$	18	13	18	Dyspnœa, headache, intercostal pain, exhaustion; symptoms had continued for many months; painful micturition at times.	No other evidence of disease could be found.	Saline cathartics, sudorifics, nitro-glycerin.	Is now apparently well.
47	6	M.	4	5	16	No	No	1020	2	9	6	18	Painful micturition for some months, extreme œdema of limbs, headache, pain in side.	Careful examination revealed no other disease.	Epsom salts, diuretics, potassii bicarb., fl. ext. buchu	Rapidly recovered, and has remained well.
48	59	M.	4	20	32	No	No	1117	$1\frac{3}{5}$	15	12	29	Has continual lumbar pain, vertigo, insomnia, exhaustion; atheromatous degeneration of arteries, œdema of limbs.	Cerebral hemorrhage after two years from first examination.	Nitro-glycerin, saline cathartics, sudorifics.	Head symptoms not much improved, but otherwise more comfortable.
49	24	F.	2	8	34	No	No	1019	1	16	8	24	Extreme dyspnœa, vertigo, exhaustion, extreme œdema of limbs, hands and face swollen; pain on passing water; symptoms had continued for months.	No discoverable disease of heart, lungs, or other organs.	Nitro-glycerin, saline cathartics, sudorifics.	Improved very rapidly, and is now well.
50	60	M.	4	8	32	No	No	1020	$1\frac{1}{2}$	14	8	28	Extreme dyspnœa; was confined to chair; feet and legs much swollen, nausea, vertigo; twitchings of muscles; pulse irregular.	Lungs and heart healthy; no other discoverable disease.	Nitro-glycerin, digitalis, saline cathartics.	Much better in 6 weeks, and has had but one or two attacks since

can often be made from this fact, but casts, like albumin, are inconstant, many patients not passing them at all, and they always appear too late to be a factor in early diagnosis.

The specific gravity of the urine is not to be relied upon unless the mean specific gravity of many specimens is taken of known quantities of urine for twenty-four hours. This would mean a small amount of urea passed within this time, since it is the dominant salt eliminated; Therefore, why not test for urea at once?

Some outward manifestations of ill health always precede for some time, often years, the passing of albumin and casts. These symptoms are in common with well-marked kidney lesions and are not due to other discoverable physical causes. Cases often, without a change in these symptoms for years, begin passing albumin and casts. It is fair to assume, therefore, that the symptoms referred to are the result of some common cause, which precedes the pronounced kidney lesions. This common cause seems to be something which produces extensive and often remote inflammations of serous membranes, which at the time, or remotely, involves the kidneys. What this cause is, we can at present only conjecture, but many of its pathological effects might be turned to advantage in early diagnosis.

Urea is excreted in abnormally small quantities in cases of well-marked kidney lesions. It is also so excreted in cases having the prominent physical symptoms without albumin and casts. It is interchangeable as a means of diagnosis with the outward signs of the disease, *i. e.*, a knowledge of the condition of ill health being also a knowledge of the amount of urea passed, and *vice versa*. Urea is excreted in small quantities months and often years before albumin and casts appear and therefore a knowledge of this excretion is invaluable as a diagnostic sign of early lesions. The diminished quantity of urea eliminated is the result of the constitutional disturbances which precede for long intervals of time the local lesion. Active treatment which would not be beneficial in other diseases having some symptoms in common, identifies this, generally relieves, and frequently apparently cures.

A brief reference to the preceding tables will doubtless make these statements more intelligible and show from what source they are derived.